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EXAMINER	
JIANG, SHAOJIA A	

ART UNIT	PAPER NUMBER
1617	

DATE MAILED: 09/26/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/554,387	FABRY, BERND	
	Examiner	Art Unit	
	Shaojia A. Jiang	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 July 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *11-32* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *11-32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This Office Action is in response to Applicant's response (remarks/Arguments) filed on July 25, 2005 wherein claims 31-32 are newly submitted.

Currently, claims 11-32 are pending in this application and under examination on the merits.

The following is new rejection(s) necessitated by Applicant's amendment filed on July 25, 2005, wherein new claims 31-32 have been added.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 31-32 as amended now new claim 26 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant's amendment submitted July 25, 2005 with respect to new claims 31-32, has been fully considered but is deemed to insert new matter into the claims since the specification as originally filed does not provide support for "an amount of from about 5 to about 10% by weight". The original specification merely discloses "0.1 to 50,

preferably 1 to 30, in particular 5 to 25 and particularly preferably 10 to 15, % by weight" (see page 8 of the specification).

The range now claimed "about 5 to about 10% by weight" is considered to the subgenus range of "0.1 to 50, preferably 1 to 30, in particular 5 to 25" as originally described in the specification. The court held that "subgenus range was not supported by generic disclosure and specific example within the subgenus range"; See, e.g., *In re Lukach*, 442 F.2d 967, 169 USPQ 795 (CCPA 1971); the court also held that "a subgenus is not necessarily described by a genus encompassing it and a species upon which it reads" (see *In re Smith*, 458 F.2d 1389,1395, 173 USPQ 679, 683 (CCPA 1972). See also MPEP 2163.

Consequently, there is nothing within the instant specification which would lead the artisan in the field to believe that Applicant was in possession of the invention as it is now claimed. See *Vas-Cath Inc. v. Mahurkar*, 19 USPQ 2d 1111, CAFC 1991, see also *In re Winkhaus*, 188 USPQ 129, CCPA 1975.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 11-18, 20-27, 30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jandacek (3,865,939 of record), Miettinen et al. (EP 0594612B1 of record), and Hasegawa et al.(English translation of record) in view of Lee et al. ("Conjugated Linoleic Acid and atherosclerosis in rabbits") or Applicant's admission regard the prior art in the specification at page 4 line 13-15, for the same reason of record stated in the Office Action dated January 26, 2005.

Jandacek discloses that phytosterols (synonymously phytostenols) have significant hypocholesterolemic activities (see col.1 lines 5-30), which meets the limitation in (i) (a) in claims 11 and 21 herein.

Jandacek also discloses that the compositions comprising phytosterols such as β–sitosterol (synonymously β-sitostenol) along with saturated and unsaturated fatty acids having from 6 to 18 carbon atoms (known to encompass double bonds) or glycerides of such fatty acids, in effective amounts from about 2.0 to about 6.0 wt.% and 0.5 to 15 wt.%, and/or combined with foodstuffs to be administered to the mammal, are useful for reducing serum cholesterol content in a mammal (see col.1 lines 5-30, col.2 lines 1-5, col.3 lines 27-28, col.4 lines 41-44, Table I, col.5 lines 17-31, Example I and claims 1, 3 and 6). The teachings of Jandacek meet the limitations, β-sitostenol and/or esters thereof recited in claims 12 and 22; the limitations, the carboxylic acid, R^1COOOH having from 6 to 18 carbon atoms in claims 13-16 and 22-26 herein, and combing foodstuff in claims 20 and 30.

Miettinen et al. teaches that β–sitosterol (β-sitostenol) and β–sitostanol and their fatty acid esters are known to be useful to lower serum cholesterol levels. See page 2

lines 5-7 and claim 1. This teaching meets the limitation in (i) (a) in claims 11-12 and 21-22 herein.

Miettinen et al. further teaches that usable fatty acids therein contain approx. 2-22 carbon atoms such as fatty acids in vegetable oil, i.e., rapeseed oil containing unsaturated fatty acids having from 2-22 carbon atoms (known to encompass double bonds). See page 3 lines 44-45 and Example 1 on page 4.

It is well known that many vegetable oils including rapeseed oil contain unsaturated fatty acids having one or more double bonds such as linoleic acid which has 18 carbons (see The Merck Index at page 5526, of record). Miettinen et al. teaches broadly the usefulness of fatty acid esters of β–sitosterol (β-sitostenol) and β–sitostanol containing approx. 2-22 carbon atoms including unsaturated fatty acid esters in the instant claimed method. This teaching meets the limitations in claims 13-16 and 22-26 herein.

Miettinen et al. further discloses that β-sitostenol fatty acid ester mixture in **combination** with rapeseed oil (containing unsaturated fatty acids having one or more double bonds such as linoleic acid, as active agents) decreased total cholesterol by 9.5% more and LDL cholesterol by 11.6% more than did rapeseed oil alone (see particularly page 4 lines 22-24). Thus, Miettinen et al. teach that the combination of phytostenol esters and fatty acids broadly including linoleic acid, is used in the instant claimed method.

Hasegawa et al. teaches that the particular fatty acid, linoleic acid, and/or phytosterol including sitosterol (sitostenol) are useful for lowering the serum cholesterol

in human mammals. The testing results in Hasegawa et al. show that linoleic acid and sitosterol in abundance contained in the vegetable oils have hypocholesteremic effects (see Table 1-5 and Figure 3-4). See also abstract and the entire article. Thus, the teachings of Hasegawa et al. teach that the **combination** of linoleic acid and sitosterol is used in the instant claimed method.

The cited prior art herein does not expressly disclose the employment of conjugated linoleic acid (CLA), as a conjugated fatty acid, in combination with a phytosterol or phytosterol esters in methods of reducing serum cholesterol content, as recited in (i) (b) in the instant claims 11, 17, 21, 27.

Lee et al. discloses that conjugated linoleic acid (CLA) significantly lowers or reduces serum the LDL cholesterol by administering CLA in the effective amounts to rabbits (see abstract, Fig 1 and 3, "Results and discussion" at page 21-22).

Applicants admit and acknowledge that "[i]t is known of conjugated linoleic acid that it has a low hypocholesteremic action" in the specification at page 4 line 13-15.

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to employ conjugated linoleic acid (CLA) in combination with a phytosterol or phytosterol esters in methods of reducing serum cholesterol content.

One having ordinary skill in the art at the time the invention was made would have been motivated to employ CLA in combination with a phytosterol or phytosterol esters in methods of reducing serum cholesterol content, since CLA is known to significantly reduce serum LDL cholesterol in animals.

Moreover, one of ordinary skill in the art would have reasonably expected that combining CLA and a phytostenol or of phytostenol esters of a fatty acid herein, all known useful for the same purpose in a composition to be administered would improve the therapeutic effect for reducing serum cholesterol content in a mammal. At least some additive therapeutic effects would have been reasonably expected. See *In re Kerkhoven*, 205 USPQ 1069 (CCPA 1980) which renders the claims prima facie obvious.

Further, the motivation for the combination of phytostenol or its esters and fatty acids broadly including conjugated linoleic acid, employed in the instant claimed method, has been clearly provided by Miettinen et al. and/or Hasegawa et al. respectively.

Thus the claimed invention as a whole is clearly prima facie obvious over the combined teachings of the prior art.

Claims 19, 28-29 and 31-32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jandacek (3,865,939 of record), Miettinen et al. (EP 0594612B1), and Hasegawa et al. in view of Lee et al. or Applicant's admission regard the prior art in the specification at page 4 line 13-15 as applied to claims 11-18, 20-27, 30, further in view of Hidevgi (US 5,277,910, of record).

The same disclosures of Jandacek, Miettinen et al., and Hasegawa et al. have been discussed above. In particular, Jandacek discloses that the amount of phytosterols

in the composition is from about 2.0 to about 6.0 wt.% and 0.5 to 15 wt.%, as pointed out above.

The cited prior art herein does not expressly the composition is in the form of gelatin capsules. The cited prior art herein does not expressly discloses that the component (a) and (b) each independently present in an amount of from about 5 to about 10% by weight.

Hidvegi discloses a similar pharmaceutical composition for the same use, lowering the blood-lipid level containing sitosterol and fatty acids such as linoleic acid formulated into gelatin capsules. See col.1 lines 59-65, col.2 line 37, col.3 line 38 and col.8 lines 18-28.

One having ordinary skill in the art at the time the invention was made would have been motivated to formulate the composition into gelatin capsules since the similar pharmaceutical composition for the same purpose, lowering the blood-lipid level, containing sitosterol and fatty acids such as linoleic acid, is known to be formulated into gelatin capsules according to Hidvegi. Formulation in various known forms is deemed within the knowledge and conventional skills in pharmaceutical art.

One having ordinary skill in the art at the time the invention was made would have been motivated to employ the component (a) and (b) in the amount of about 5 to about 10% by weight, since the determination or optimization of known amounts of the known component (a) and (b), in a composition based on the prior art teachings, is considered well within conventional skills in pharmaceutical science, involving merely routine skill in the art.

It has been held that it is within the skill in the art to select optimal parameters, such as amounts of ingredients, in a composition in order to achieve a beneficial effect. See *In re Boesch*, 205 USPQ 215 (CCPA 1980).

Claims 11-32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jandacek (3,865,939 of record), Miettinen et al. (EP 0594612B1 of record), and Hasegawa et al.(English translation of record) in view of Pariza et al. (US 5,837,733, PTO-892), further in view of Hidevgi (US 5,277,910, of record).

The same disclosures of Jandacek, Miettinen et al., Hasegawa et al. and Hidvegi have been discussed in the 103(a) rejections above.

The cited prior art herein does not expressly disclose the employment of a conjugated fatty acid, e.g., conjugated linoleic acid (CLA), in lieu of linoleic acid (LA), in combination with a phytosterol or phytosterol esters in methods of reducing serum cholesterol content.

The cited prior art herein does not expressly the composition is in the form of gelatin capsules. The cited prior art herein does not expressly discloses that the component (a) and (b) each independently present in an amount of from about 5 to about 10% by weight.

Pariza et al. discloses that conjugated linoleic acid (CLA) significantly lowers or reduces much more serum apolipoprotein B secretion in animals than linoleic acid (LA) does according to the testing results therein (see Fig 1, col.2 line 34-37; "Results" at

col.4 line 65 to col.5 line 27). Apolipoprotein B secretion is known to associate or increase so-called "bad" cholesterols, VLDL and LDL cholesterols (see col.1 lines 17-26); thus CLA reduces "bad" cholesterols, VLDL and LDL via reducing apolipoprotein B secretion in the blood. Hence, Pariza et al. teaches that CLA is much more effective than LA in reducing serum "bad" cholesterols through reducing apolipoprotein B secretion in animals. Pariza et al. also disclose the administration of CLA in the effective amounts to an animal or mammal (see col.9 line 20-47 and claims 1-10).

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to employ conjugated linoleic acid (CLA) in lieu of linoleic acid (LA) in the claimed methods of reducing serum cholesterol content.

One having ordinary skill in the art at the time the invention was made would have been motivated to employ CLA in lieu of LA in the claimed methods of reducing serum cholesterol content, since CLA is known to be much more effective than LA in reducing serum "bad" cholesterols through reducing apolipoprotein B secretion in animals.

Therefore, the property and benefit of CLA over LA in reducing serum "bad" cholesterols through reducing apolipoprotein B secretion in animals, have clearly provided the motivation of the claimed invention.

Moreover, one of ordinary skill in the art would have reasonably expected that combining a fatty acid such as CLA and a phytostenol or of phytostenol esters of a fatty acid herein, all known useful for the same purpose in a composition to be administered would improve the therapeutic effect for reducing serum cholesterol content in a

mammal. At least some additive therapeutic effects would have been reasonably expected. See *In re Kerkhoven*, 205 USPQ 1069 (CCPA 1980) which renders the claims prima facie obvious.

Further, the motivation for the combination of phytostenol esters and fatty acids broadly including linoleic acid and also including conjugated linoleic acid, employed in the instant claimed method, has been provided by Miettinen et al. and/or Hasegawa et al. respectively.

Furthermore, formulating the composition into gelatin capsules is deemed obvious since the similar pharmaceutical composition for the same purpose, lowering the blood-lipid level, containing sitosterol and fatty acids such as linoleic acid is known to be formulated into gelatin capsules according to Hidvegi.

One having ordinary skill in the art at the time the invention was made would have been motivated to employ the component (a) and (b) in the amount of about 5 to about 10% by weight, since the determination or optimization of known amounts of the known component (a) and (b), in a composition based on the prior art teachings, is considered well within conventional skills in pharmaceutical science, involving merely routine skill in the art.

It has been held that it is within the skill in the art to select optimal parameters, such as amounts of ingredients, in a composition in order to achieve a beneficial effect. See *In re Boesch*, 205 USPQ 215 (CCPA 1980).

Thus the claimed invention as a whole is clearly prima facie obvious over the combined teachings of the prior art.

Response to Argument

Applicant's arguments filed July 25, 2005 with respect to the rejections made under 35 U.S.C. 103(a) of record in the previous Office Action January 26, 2005 have been fully considered but are not deemed persuasive as to the nonobviousness of the claimed invention over the prior art as further discussed below.

Applicant asserts that neither Lee nor the cited disclosure in Applicant's specification support the Examiner's position that at the time of the invention, it was known that CLA reduced cholesterol.

Contrary to Applicant's assertion, Lee et al. discloses that conjugated linoleic acid (CLA) significantly lowers or reduces serum the LDL cholesterol by administering CLA in the effective amounts to rabbits, demonstrated by Fig 1 and 3, see also "Results and discussion" at page 21-22.

Applicants admit and acknowledge by stating in the specification at page 4 line 13-15 that "[i]t is known of conjugated linoleic acid that it has a low hypocholesteremic action".

Applicant also asserts that the holding *In re Kerkhoven* is inapplicable to the particular facts in issue here.

Contrary to Applicant's assertion, in this case, Jandacek, Miettinen et al., and Hasegawa et al., all disclose that the **combination** of phytosterols or phytosterol esters, **and** unsaturated fatty acids having from 6 to 18 carbon atoms such as linoleic acid (LA) are useful for reducing serum cholesterol content in a mammal. Thus, the motivation to combine phytosterols or phytosterol esters, **and** fatty acids, has been clearly provided

by Jandacek, Miettinen et al., and Hasegawa et al. Moreover, CLA is known to significantly reduce serum LDL cholesterol in animals according to Lee.

Pariza et al. also discloses that conjugated linoleic acid (CLA) significantly lowers or reduces much more serum apolipoprotein B secretion in animals than linoleic acid (LA) does according to the testing results therein (see Fig 1, col.2 line 34-37; "Results" at col.4 line 65 to col.5 line 27). Apolipoprotein B secretion is known to associate or increase so-called "bad" cholesterols, VLDL and LDL cholesterols (see col.1 lines 17-26); thus CLA reduces "bad" cholesterols, VLDL and LDL via reducing apolipoprotein B secretion in the blood. Hence, Pariza et al. teaches that CLA is much more effective than LA in reducing serum "bad" cholesterols through reducing apolipoprotein B secretion in animals. Pariza et al. also disclose the administration of CLA in the effective amounts to an animal or mammal (see col.9 line 20-47 and claims 1-10).

Therefore, the property and benefit of CLA over LA in reducing serum "bad" cholesterols through reducing apolipoprotein B secretion in animals, have clearly provided the motivation of the claimed invention. Thus, using CLA as a specific fatty acid in the known combinations of Jandacek, Miettinen et al., or Hasegawa et al. is clearly obvious to one of ordinary skill in the art.

It must be recognized that any judgment on obviousness takes into account knowledge which was generally available and within the level of ordinary skill at the time the claimed invention was made.

Moreover, it has been held that it is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for same purpose in

order to form a third composition that is to be used for the very same purpose; idea of combining them flows logically from their having been individually taught in prior art. *In re Kerkhoven*, 205 USPQ 1069, CCPA 1980. See MPEP 2144.06.

Applicant's arguments regarding the claimed significantly improved results in Applicant's data of Examples and Table 1 in the specification at pages 8-9 have been fully considered with respect to the nonobviousness and/or unexpected results of the claimed invention over the prior art but are not deemed persuasive for the reasons below. It is noted that lauric acid in lauric acid β–sitostanol ester or lauric acid β–sitostenol ester employed in the testing herein is not even an unsaturated carboxylic acid (having no double bond), which is **not** the instant preferred carboxylic acid having up to 3 double bonds (see claims 13-14 herein).

The results on the tests of the employment of β–sitostenol, β–sitostanol, or their esters, combined with conjugated linoleic acid in the composition administered to rats in Table 1 in the specification, showing some additive effects on reducing the cholesterol content in rats, would be *expected* based on the teachings of all primary references in combined with the disclosure of Lee or Pariza et al., as discussed above.

Moreover, at least additive therapeutic effects would have been reasonably expected based on the well settled principle set forth *In re Kerkhoven* regarding combination inventions. Therefore, the results herein are clearly expected and not unexpected based on the cited prior art. Expected beneficial results are evidence of obviousness. See MPEP § 716.02(c).

Furthermore, the tests herein merely employ the combination of two particular phytostenols, β–sitostenol or β–sitostanol in combination with the particular conjugated fatty acid, conjugated linoleic acid. Thus, the evidence in the testing is not commensurate in scope with the claimed invention and does not demonstrate criticality of a claimed range of phytostenol compounds and conjugated fatty acids herein. See MPEP § 716.02(d).

Therefore, no clear and convincing evidence of nonobviousness or unexpected results for the combination of a phytostenol or its ester and a conjugated fatty acid in the claimed method presented in specification herein is seen to support the nonobviousness of the instant claimed invention over the prior art of record.

In view of the rejections to the pending claims set forth above, no claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner Jiang, whose telephone number is (571)272-0627. The examiner can normally be reached on Monday-Friday from 9:00 to 5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan, Ph.D., can be reached on (571)272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

S. Anna Jiang, Ph.D.
Primary Examiner
Art Unit 1617
September 21, 2005